REMARKS

Applicants respectfully request entry of amendments to claims 1, 4, 5, 8-11, 14, 18, 23, 24, and 26. Please withdraw claims 20-22 and 27-67, without prejudice or disclaimer. Support for the amendments can be found throughout the specification, including paragraphs [0011], [0013], [0040], [0063], [0083]-[0085], [0089], [0097], Figure 9, and the originally filed claims and, therefore, do not add new matter.

Applicants submit that pending claims 1-19 and 23-26 are in condition for allowance, and respectfully request that the claims as amended be entered.

Objections

Applicants have provided herewith a corrected Figure 5 and 7A.

Applicants have provided herewith corrections to the specification to amend the recitations of trademarks, where such trademarks have been capitalized and accompanied by generic terminology.

Regarding claims 10, 23, 24, and 26, Applicants have corrected the claims as suggested in the Action.

For these reasons, Applicants respectfully request that the objections be withdrawn.

Rejections Under 35 U.S.C. §112, Second Paragraph

Claims 1-19 and 23-26 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite

Applicants traverse the rejection as it might apply to the amended claims, including claims dependent therefrom, for the reasons given below.

Claim 1 no longer recites "suitable MHC-binding peptide" so this aspect of the rejection is rendered moot. Applicants have amended the claim to recite "MHC-binding peptide." The term "MHC binding peptide" is a term of art and would be known to one of skill in the art generally as peptide of 8 to 10 amino acids in length, which is stably bound to MHC at its two ends by contacts between atoms in the free amino and carboxy termini and invariant sites that are found at each end of the peptide binding groove of all MHC class molecules (see, e.g., Janeway

et al., Immunobiology: The Immune System in Health and Disease, (1999) 4th Ed., Cpt. 4, pp. 120-121, Garland Publishing, New York, NY). Further, one of skill in the art would know the meaning of the term as it is art recognized in the patent literature (e.g., see U.S. Pat. No. 5,635,363, at col. 5, ll. 29-31). Moreover, one of skill in the art of immunology, to which this invention belongs, would know these properties. Moreover, these properties are recited at paragraph [0076] of the instant application, as well as throughout the specification. As such, one of skill in the art would understand the metes and bounds of the term.

Regarding the terms "one or more" and article "the" in claim 1, while not acquiescing to the reasoning offered in the Action, in order to expedite prosecution toward allowance, the claim has been amended to more readily identify the species.

Claims 2, 11, 14, and 18 are alleged to be indefinite for reciting the terms "reconstituting conditions," denaturing conditions," and/or "renaturing conditions." Applicants respectfully submit that the examiner is incorrect. Review of the specification demonstrates that these terms are defined and exemplified in the specification as filed. For example, in Example 3, paragraphs [0117]-[0123] reconstitution is clearly demonstrated, including the use of appropriate pH, use of beta 2 microglobulin, temperature ranges, as well as appropriate buffers as defined at paragraph [0095] of the specification. Further, denaturation conditions are defined at paragraph [0011], and can be exemplified by the recitations concerning "stripping" (see, e.g., paragraphs [0087], [0116], and [0152], which describe that basically denaturation involves the use of low pH to remove native binding peptides from MHC molecules). Moreover, renaturing conditions are also defined, (see paragraph [0081], which includes the presence of a MHC binding peptide, a refolding buffer, having a pH from about 7 to about 8.5, and the presence of beta-2 microglobulin: this method, again is exemplified in Example 3, paragraphs [0117]-[0123]).

Applicants submit that indefiniteness analysis requires whether those skilled in the art would understand what is claimed when read in light of the specification (see, e.g., Morton International, Inc. v. Cardinal Chemical Co., 28 U.S.P.Q.2d 1190 (Fed. Cir. 1993), and given that the disputed terms would have definite meaning when construed in the light of the specification, one of skill in the art would understand the metes and bounds of the claims.

Claim 11 is alleged to be indefinite because it recites "reconstitutes" (claims 13, 17, 18, and 26 are also cited). Reconstituting conditions has been defined as outlined above, and thus a reconstituted monomer would be construed from the recitations as cited. Regarding claim 11, the term "reconstitutes to incorporate" has been amended to recite "refolds to incorporate." Refolding as a way of reconstituting monomers is expressly recited in paragraph [0018] as filed. Thus, one of skill in the art would understand the metes and bounds of the claim.

Claim 5 is alleged to be indefinite for reciting that the solid surface is "suitable for screening in a high throughput system." While not acquiescing to the reasoning offered in the Action, in order to expedite prosecution toward allowance, the claim has been amended to recite a property that results from binding of the MHC to the solid surface. As this property is clearly supported in the specification at paragraph [0011], one of skill in the art would understand the metes and bounds of the claim.

Claim 14 is alleged to lack proper antecedent basis. While not acquiescing to the reasoning offered in the Action, in order to expedite prosecution toward allowance, the claim has been amended to change its dependency to correct the antecedent issue.

Claim 8 is alleged to lack an essential step. While not acquiescing to the reasoning offered in the Action, in order to expedite prosecution toward allowance, the claim has been amended to clarify the positive process step as claimed.

Claim 9 is alleged to recite trademarks/trade names Neutravidin and Streptactin, and are thus indefinite. Applicants respectfully submit that M.P.E.P. §608.01(v) states:

> Names used in trade are permissible in patent applications if:
>
> (A) Their meanings are established by an accompanying definition which is sufficiently precise and definite to be make a part of a claim or
>
> (B) In this country, their meanings are well-known and satisfactorily defined in the literature.
>
> Conditions (A) or (B) must be met at the time of filing of the complete application.

A brief search of the USPTO database using "streptactin" as the keyword, limiting the search to claims results in two hits (U.S. Pat. Nos.: 7,163,633 and 6,887,377), both of which

were filed at the time the present application was filed. Further, a brief search of the USPTO database using "streptactin" as the keyword, limiting the search to claims results in twenty-six hits, at least two of which have issue dates in the 1990's (e.g., U.S. Pat. Nos.: 5,798,273 and 5,776,487). As such, these terms meet conditions (A) and (B), and one of skill in the art would know that the names point to the product, and not to one producer, and thus, the use of the names is permissible.

Claim 19 is alleged to be indefinite for reciting the term "B9.12.1." The antibody denoted by the term at issue is a commercially available product (see, Exhibit A, attached) and has been known since 1988 (see, Perarnau, B. M., A. C. Gillet, R. Hakem, M. Barad, F. A. Lemonnier. 1988. Human $ß_2$-microglobulin specifically enhances cell-surface expression of HLA class I molecules in transfected murine cells. J Immunol 141:1383.). As such, one of skill in the art would know the metes and bounds of the claim.

For these reasons, Applicants respectfully request that the rejection be withdrawn.

Rejections Under 35 U.S.C. §112, First Paragraph

Claims 1-19 and 23-26 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking written description support.

Applicants traverse the rejection as it might apply to the amended claims, including claims dependent therefrom, for the reasons given below.

The Office Action alleges, in pertinent part, that as the specification does not disclose sufficient information to support the genera of modified MHC monomers and suitable MHC-binding peptides. As the amended claims no longer recite "modified MHC monomer" and "suitable MHC-binding peptide," these aspects of the rejection are rendered moot.

The Action further intimates that conformational epitopes and monoclonal antibodies which specifically bind to a reconstituted monomer, and not to a denatured monomer, do not meet the standard for adequate written description. Applicants respectfully submit that such allegations are incorrect.

The position taken in the Office Action in view of the cited case law is inapposite in that none of the cases recited in the Action support a written description standard which requires a re-description of what was already known. For example, in University of California v. Eli Lilly and Co., 43 U.S.P.Q.2d 1398 (Fed. Cir. 1997), much of the DNA sought to be claimed was considered an indication of a result that one might achieve if one made that invention. In Enzo Biochemical, Inc. v. Gen-Probe Inc., 63 U.S.P.Q.2d 1609 (Fed. Cir. 2002), the court explained that an invention may be described by disclosure of sufficiently detailed, relevant identifying characteristics, including, inter alia, functional characteristics when coupled with a known or disclosed correlation between function and structure, which the patentee could not establish. For the instant invention there are no claims by result, and the structures and functions of MHCs, including MHC-binding peptides, were already known. Thus, the present facts are distinguishable.

On the other hand, in Capon v. Eshhar, 76 U.S.P.Q.2d 1078, 1085, 418 F.3d 1349, at 1357 (Fed. Cir. 2005), the court reasoned that when the prior art includes structure and function information, there is no *per se* rule that the information must be determined afresh. As in Capon, the present invention is not in the discovering of which MHC monomers or binding peptides of some unknown or "wished for" sequence might be related to a specific function, but in the novel combination of the element of known components to achieve a novel result (Id., at 1357). Thus, in concurrence with the Court of Appeals for the Federal Circuit in Capon, Applicant submits that the requirement that a system of polypeptides prepared from known sequences of known function must be analyzed and reported in the specification is not the standard for written description. Id.

Regarding conformational epitopes, data for linear and discontinuous epitopes have been available since 1986 (see, e.g., Barlow et al., Continuous and discontinuous protein antigenic determinants. Nature (1986) 322(6081):747-748). Further, databases for such epitopes have been available since 1998 (see, e.g., Brusic et al., MHCPEP, a database of MHC binding peptides: update. Nuc Acid Res (1998) 26(1):368-371; Rammensee et al., SYFPEITHI: database for MHC ligands and peptide motifs. Immunogenetics (1999) 50(3-4):213-219). In fact, a database limited to only conformational epitopes can be accessed at http://web.kuicr.kyoto-

u.ac.jp/~ced. And as stated for B9.12.1 above, antibodies which bind to conformational epitopes were commercially available and/or were generally known at the time the invention was filed (e.g., see Özyörük et al., Monoclonal antibodies to conformational epitopes of the surface glycoprotein of caprine arthritis-encephalitis virus: potential application to competitive enzyme-linked immunosorbent assay for detecting antibodies in goat sera. Clin and Diag Lab Immunol (2001) 8(1):44-51; Allander et al., Recombinant human monoclonal antibodies against different conformational epitopes of the E2 envelope glycoprotein of hepatitis C virus that inhibit its interaction with CD81. J Gen Virol (2000) 81:2451-2459; Craven et al., Monoclonal antibodies specific for the empty conformation of HLA-DR1 reveal aspect of the conformational change associated with peptide binding. J Biol Chem (2004) 279(16):16561-16570).

Accordingly, because 1) MHC monomers as claimed were know in the art, 2) MHC binding peptides were art defined and art recognized (see, e.g., Janeway et al., Immunobiology: The Immune System in Health and Disease, (1999) 4th Ed., Cpt. 4, pp. 120-121, Garland Publishing, New York, NY), and 3) antibodies against conformational epitope were also known, including antibodies that were commercially available, one of skill in the art could envision the chemical details of the elements of the claimed invention, and would appreciate that the inventors were in possession of the genus as claimed at the time the invention was filed.

For these reasons, Applicants respectfully request that the rejection be withdrawn.

Claims 1-19 and 23-26 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement.

Applicants traverse the rejection as it might apply to the amended claims, including claims dependent therefrom, for the reasons given below.

The Office Action alleges, in pertinent part, that while the specification is enabling for one or more MHC monomers or a system comprising the antibody B9.12.1, this does not reasonably provide enablement for modified MHC monomers or antibodies that bind reconstituted but not denatured monomers.

The amended claims no longer recite "modified monomers," but recite that the "modified MHC monomer is a chimeric monomer comprising human and murine MHC domains."

However, the Action goes on to allege that the specification as filed does not enable 1) complete reconstitution of monomers and 2) suitable MHC-binding peptides. The Action further intimates that due to the unpredictability of protein chemistry, undue experimentation would be required for the skilled artisan to practice the full scope of the invention. Applicants respectfully submit that such allegations are incorrect.

While it is appropriate to recognize variability in determining the scope of invention, determination of what is needed to support generic claims to biological subject matter depends on a variety of factors including 1) knowledge in the particular field, 2) the extent and content of the prior art, 3) the maturity of the science or technology, and 4) the predictability of the aspect at issue. Capon v. Eshhar, 76 U.S.P.Q.2d 1078, 1084, 418 F.3d 1349, at 1356 (Fed. Cir. 2005).

The present invention represents more than "a mere germ of an idea," the specification supplies the novel aspects of the invention, and identification of MHC binding peptides is certainly not in the early stages of development (e.g., page 4, paragraphs [0012] and [0013]). (See, also, Genentech, Inc. v. Novo Nordisk, 42 U.S.P.Q.2d 101, 108 F.3d 1361 (Fed. Cir. 1997)). Further, in the present specification, not only are the general teachings of how to select and recombine the requisite domains for producing chimeric MHC presented (e.g., FIG. 9), but also specific examples are provided for the production of chimeric structures using mouse and human domains (e.g., paragraphs [0040], [0063], [0084], [0085], and [0089]). Moreover, standardized description and identification, including selecting, isolating, and linkage of well recognized domains, whose structure/function relationships are known, are disclosed (e.g., paragraphs [0063] and [0084]). And while such procedures involve some level of technical manipulation, because such methods and steps are routinely used in the art, such procedures do not rise to the level of undue experimentation. (See, e.g., Johns Hopkins University v. Cellpro, Inc., 47 U.S.P.Q.2d 1705, 152 F.3d 1342 (Fed. Cir. 1998), where the court stated that "experimentation does not constitute undue experimentation" where "it is merely routine.").

Regarding unpredictability and 100% reconstitution of the MHC monomer, it is not necessary that every permutation within a generally operable invention be effective in order for an inventor to obtain a generic claim, provided that the effect is sufficiently demonstrated to characterize the generic invention. See, e.g., In re Angstadt, 537 F.2d 498, 504 (CCPA 1976).

Accordingly, generic inventions are not *per se* invalid because success for each possible iteration is not assured. Capon, at 1357. Further, the idea that 100% of the MHC monomers may not reconstitute is directed to efficacy, and efficacy is not the standard for enablement (see, e.g., Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd., 18 U.S.P.Q.2d 1016 (Fed. Cir. 1991)).

Applicants further submit that it is well established that antigenic determinants may be composed of discontinuous epitopes (i.e., conformational) and linear epitopes (see, e.g., Janeway et al., Immunobiology: The Immune System in Health and Disease, (1999) 4th Ed., Cpt. 3, p. 88, Garland Publishing, New York, NY). Clearly, given the level of skill of the artisan in the immunology arts, to suggest that making and using an antibody which distinguishes between a native and denatured form of the same protein represents undue experimentation would seem to presume that the specification is written to enable a layperson, and not those skilled in the art to, to practice the claimed invention (*cf.*, Ajinomoto Co., Inc. v. Archer-Daniels-Midlands Co., 56 U.S.P.Q.2d 1332 (Fed. Cir. 2000)).

Therefore, the claims are enabled because the specification provides appropriate guidance and prediction of function based on observed properties of the claimed polypeptide elements such that one of skill in the art could practice the invention as claimed, in the absence of undue experimentation.

For these reasons, Applicants respectfully request that the rejection, including as it may be applied to the amended claims, be withdrawn.

Rejection Under 35 U.S.C. §102

Claims 1-5, 8-12, and 14-16 stand rejected under 35 U.S.C. §102(b), as allegedly being anticipated by Altman et al.

Applicants traverse the rejection as it might apply to the amended claims, including claims dependent therefrom, for the reasons given below.

The Office Action alleges, in pertinent part, that the cited reference teaches the elements as recited in the present claims.

The present claims expressly recite that the bound monomer incorporates from solution a MHC binding peptide. In other words, the monomer binds to the MHC binding peptide after the monomer is bound to the solid surface. This can also be seen in the Examples at p. 31, Table 1.

Altman et al. teach that the monomer has the formula (α-β-P)n (see, col. 3, ll. 20-21 and col. 5, ll. 65-66). α is defined as an α chain of a class I or class II MHC protein (see, col. 3, ll. 21-22). β is defined as a β chain of a class II MHC protein or β_2 microglobulin for a MHC class I protein (see, col. 3, ll. 22-24). P is defined as a peptide antigen (see, col. 3, ll. 24-25). Altman et al. goes on to recite that the monomer with a biotinylated binding partner, may be attached to an insoluble support. As such, Altman et al. do not teach that the bound monomer incorporates from solution a MHC binding peptide, and cannot teach this element because the binding site of the immobilized MHC monomer is occupied by the peptide.

As stated in Hybritech Inc. v. Monoclonal Antibody, Inc., 231 U.S.P.Q. 81 (Fed. Cir. 1986), "It is axiomatic that for prior art to anticipate under 102 it has to meet every element of the claimed invention."

Therefore, because the instant claims recite that the solid surface bound monomer incorporates from solution a MHC binding peptide, the Altman et al. reference does not anticipate the claimed invention.

Failure of the prior art to meet every element of the claimed invention does not meet the standard under §102. For these reasons, Applicants respectfully request that the rejection be withdrawn.

Rejections Under 35 U.S.C. §103

Claims 6-7 stand rejected under 35 U.S.C. §103(a), as allegedly being unpatentable over Altman et al. in view of Becker et al.

Applicants traverse the rejection as it might apply to the amended claims, including claims dependent therefrom, for the reasons given below.

Applicants submit that because the cited references do not teach all the claim limitations, one of skill in the art would not be motivated to combine the reference teachings.

The Office Action alleges, in pertinent part, that Altman et al. is silent with respect to teaching that the monomer is attached reversibly or by a cleavable linkage. The Action then provides Becker et al. to cure the deficiency identified in the primary reference. However, Becker et al. does not teach that the solid surface bound monomer incorporates from solution a MHC binding peptide, an element presently recited in the claims.

Applicants submit that, in fact, the Altman et al. reference "teaches away" from the present invention. One of skill in the art would only extract from such a teaching that the MHC binding peptide is bound to the monomer when attached to the solid surface. As such, the reference does not teach the purpose of incorporation of a MHC binding peptide from solution, and thus, the purpose of Applicants' invention could not be accomplished using the teachings of the cited reference. Therefore, the reference teaches away, since the impression left to the skilled artisan is that the product would not have the property sought by Applicants. In re Caldwell, 319 F.2d 254, 256; 138 U.S.P.Q. 243, 245 (CCPA 1963).

Applicants submit, not merely as a theoretical proposition, that because the incorporation from solution is ultimately necessary *as a requisite property* of the present invention, in view of the teachings of Altman et al. becomes an impossibility.

Further, as there is no suggestion or expectation of success regarding incorporating MHC binding peptides from solution, whether Becker et al. teach or do not teach reversible immobilization is immaterial.

It is axiomatic that one cannot simple use the Applicant's disclosure as a "blueprint" to reconstruct, by hindsight, Applicant's claim. See, e.g., Interconnect Planning Corp. v. Feil, 774 F.2d 1132, 227 U.S.P.Q. 543 (Fed. Cir. 1985). Because there is neither the suggestion nor expectation of success that can be found in the cited art, no *prima facie* case of obviousness has been established.

Because the teachings of Altman et al. would not result in the claimed invention when combined with the teachings of Becker et al., one of skill in the art would not have an expectation of success since the invention as claimed would not be achieved in view of such teachings. Therefore, one of skill in the art would not be motivated to combine such teachings.

Applicants submit that because there is no reasonable expectation of successfully achieving the invention as claimed, there is no motivation to combine the cited references, thus, no *prima facie* case for obviousness exists. For these reasons, Applicants respectfully request that the rejection, including as it might be applied against the amended claims, be withdrawn.

Claims 13, 17, and 18 stand rejected under 35.U.S.C. §103(a), as allegedly being unpatentable over Altman et al. in view of Jager et al.

Applicants traverse the rejection as it might apply to the amended claims, including claims dependent therefrom, for the reasons given below.

Applicants submit that because the cited references do not teach all the claim limitations, one of skill in the art would not be motivated to combine the reference teachings.

The Office Action alleges, in pertinent part, that Altman et al. is silent with respect to teaching a monoclonal antibody that binds to the reconstituted, but not the denatured form of the MHC monomer. The Action then provides Jager et al. to cure the deficiency identified in the primary reference. However, Jager et al. does not teach that the solid surface bound monomer incorporates from solution a MHC binding peptide, an element presently recited in the claims.

Applicants submit that, in fact, the Altman et al. reference "teaches away" from the present invention. One of skill in the art would only extract from such a teaching that the MHC binding peptide is bound to the monomer when attached to the solid surface. As such, the reference does not teach the purpose of incorporation of a MHC binding peptide from solution, and thus, the purpose of Applicants' invention could not be accomplished using the teachings of the cited reference. Therefore, the reference teaches away, since the impression left to the skilled artisan is that the product would not have the property sought by Applicants. In re Caldwell, 319 F.2d 254, 256, 138 U.S.P.Q. 243, 245 (CCPA 1963).

Applicants submit, not merely as a theoretical proposition, that because the incorporation from solution is ultimately necessary *as a requisite property* of the present invention, in view of the teachings of Altman et al. becomes an impossibility.

Further, as there is no suggestion or expectation of success regarding incorporating MHC binding peptides from solution, whether Jager et al. teach or do not teach methods for detecting interaction of T cells with MHC molecules using a monoclonal antibody is immaterial.

It is axiomatic that one cannot simple use the Applicant's disclosure as a "blueprint" to reconstruct, by hindsight, Applicant's claim. See, e.g., Interconnect Planning Corp. v. Feil, 774 F.2d 1132, 227 U.S.P.Q. 543 (Fed. Cir. 1985). Because there is neither the suggestion nor expectation of success that can be found in the cited art, no *prima facie* case of obviousness has been established.

Because the teachings of Altman et al. would not result in the claimed invention when combined with the teachings of Jager et al., one of skill in the art would not have an expectation of success since the invention as claimed would not be achieved in view of such teachings. Therefore, one of skill in the art would not be motivated to combine such teachings.

Applicants submit that because there is no reasonable expectation of successfully achieving the invention as claimed, there is no motivation to combine the cited references, thus, no *prima facie* case for obviousness exists. For these reasons, Applicants respectfully request that the rejection, including as it might be applied against the amended claims, be withdrawn.

Claims 13, 17, and 18 stand rejected under 35 U.S.C. §103(a), as allegedly being unpatentable over Altman et al. in view of Hildebrand et al.

Applicants traverse the rejection as it might apply to the amended claims, including claims dependent therefrom, for the reasons given below.

Applicants submit that because the cited references do not teach all the claim limitations, one of skill in the art would not be motivated to combine the reference teachings.

The Office Action alleges, in pertinent part, that Altman et al. is silent with respect to teaching a monoclonal antibody that binds to the reconstituted, but not the denatured form of the MHC monomer. The Action then provides Hildebrand et al. to cure the deficiency identified in the primary reference. However, Hildebrand et al. does not teach that the solid surface bound monomer incorporates from solution a MHC binding peptide, an element presently recited in the claims.

Applicants submit that, in fact, the Altman et al. reference "teaches away" from the present invention. One of skill in the art would only extract from such a teaching that the MHC binding peptide is bound to the monomer when attached to the solid surface. As such, the reference does not teach the purpose of incorporation of a MHC binding peptide from solution, and thus, the purpose of Applicants' invention could not be accomplished using the teachings of the cited reference. Therefore, the reference teaches away, since the impression left to the skilled artisan is that the product would not have the property sought by Applicants. In re Caldwell, 319 F.2d 254, 256, 138 U.S.P.Q. 243, 245 (CCPA 1963).

Applicants submit, not merely as a theoretical proposition, that because the incorporation from solution is ultimately necessary *as a requisite property* of the present invention, in view of the teachings of Altman et al. becomes an impossibility.

Further, as there is no suggestion or expectation of success regarding incorporating MHC binding peptides from solution, whether Hildebrand et al. teach or do not teach methods for detecting interaction of T cells with MHC molecules using a monoclonal antibody is immaterial.

It is axiomatic that one cannot simple use the Applicant's disclosure as a "blueprint" to reconstruct, by hindsight, Applicant's claim. See, e.g., Interconnect Planning Corp. v. Feil, 774 F.2d 1132, 227 U.S.P.Q. 543 (Fed. Cir. 1985). Because there is neither the suggestion nor expectation of success that can be found in the cited art, no *prima facie* case of obviousness has been established.

Because the teachings of Altman et al. would not result in the claimed invention when combined with the teachings of Hildebrand et al., one of skill in the art would not have an expectation of success since the invention as claimed would not be achieved in view of such teachings. Therefore, one of skill in the art would not be motivated to combine such teachings.

Applicants submit that because there is no reasonable expectation of successfully achieving the invention as claimed, there is no motivation to combine the cited references, thus, no *prima facie* case for obviousness exists. For these reasons, Applicants respectfully request that the rejection, including as it might be applied against the amended claims, be withdrawn.

Claim 19 stands rejected under 35 U.S.C. §103(a), as allegedly being unpatentable over Altman et al. in view of Jager et al., or alternatively, Altman et al. in view of Hildebrand et al., and in further view of Martin et al.

Applicants traverse the rejection as it might apply to the amended claims, including claims dependent therefrom, for the reasons given below.

Applicants submit that because the cited references do not teach all the claim limitations, one of skill in the art would not be motivated to combine the reference teachings.

The Office Action alleges, in pertinent part, that Altman et al. in view of Jager et al. or Hildebrand et al. is silent with respect to teaching the antibody produced by B9.12.1. The Action then provides Martin et al. to cure the deficiency identified in the primary references. However, Martin et al. does not teach that the solid surface bound monomer incorporates from solution a MHC binding peptide, an element presently recited in the claims.

Applicants submit that, in fact, the Altman et al. reference "teaches away" from the present invention. One of skill in the art would only extract from such a teaching that the MHC binding peptide is bound to the monomer when attached to the solid surface. As such, the reference does not teach the purpose of incorporation of a MHC binding peptide from solution, and thus, the purpose of Applicants' invention could not be accomplished using the teachings of the cited reference. Therefore, the reference teaches away, since the impression left to the skilled artisan is that the product would not have the property sought by Applicants. In re Caldwell, 319 F.2d 254, 256, 138 U.S.P.Q. 243, 245 (CCPA 1963).

Applicants submit, not merely as a theoretical proposition, that because the incorporation from solution is ultimately necessary *as a requisite property* of the present invention, in view of the teachings of Altman et al. becomes an impossibility.

Further, as there is no suggestion or expectation of success regarding incorporating MHC binding peptides from solution, whether Martin et al. teach or do not teach B9.12.1 is immaterial.

It is axiomatic that one cannot simple use the Applicant's disclosure as a "blueprint" to reconstruct, by hindsight, Applicant's claim. See, e.g., Interconnect Planning Corp. v. Feil, 774 F.2d 1132, 227 U.S.P.Q. 543 (Fed. Cir. 1985). Because there is neither the suggestion nor

expectation of success that can be found in the cited art, no *prima facie* case of obviousness has been established.

Because the teachings of Altman et al. would not result in the claimed invention when combined with the teachings of Jager et al., Hildebrand et al., or Martin et al., one of skill in the art would not have an expectation of success since the invention as claimed would not be achieved in view of such teachings. Therefore, one of skill in the art would not be motivated to combine such teachings.

Applicants submit that because there is no reasonable expectation of successfully achieving the invention as claimed, there is no motivation to combine the cited references, thus, no *prima facie* case for obviousness exists. For these reasons, Applicants respectfully request that the rejection, including as it might be applied against the amended claim, be withdrawn.

Claims 23 and 24 stand rejected under 35 U.S.C. §103(a), as allegedly being unpatentable over Altman et al. in view of Zuk et al.

Applicants traverse the rejection as it might apply to the amended claims, including claims dependent therefrom, for the reasons given below.

Applicants submit that because the cited references do not teach all the claim limitations, one of skill in the art would not be motivated to combine the reference teachings.

The Office Action alleges, in pertinent part, that Altman et al. is silent with respect to teaching a kit. The Action then provides Zuk et al. to cure the deficiency identified in the primary reference. However, Zuk et al. does not teach that the solid surface bound monomer incorporates from solution a MHC binding peptide, an element presently recited in the claims.

Applicants submit that, in fact, the Altman et al. reference "teaches away" from the present invention. One of skill in the art would only extract from such a teaching that the MHC binding peptide is bound to the monomer when attached to the solid surface. As such, the reference does not teach the purpose of incorporation of a MHC binding peptide from solution, and thus, the purpose of Applicants' invention could not be accomplished using the teachings of the cited reference. Therefore, the reference teaches away, since the impression left to the skilled

artisan is that the product would not have the property sought by Applicants. In re Caldwell, 319 F.2d 254, 256, 138 U.S.P.Q. 243, 245 (CCPA 1963).

Applicants submit, not merely as a theoretical proposition, that because the incorporation from solution is ultimately necessary *as a requisite property* of the present invention, in view of the teachings of Altman et al. becomes an impossibility.

Further, as there is no suggestion or expectation of success regarding incorporating MHC binding peptides from solution, whether Zuk et al. teach or do not teach methods for detecting interaction of T cells with MHC molecules using a monoclonal antibody is immaterial.

It is axiomatic that one cannot simple use the Applicant's disclosure as a "blueprint" to reconstruct, by hindsight, Applicant's claim. See, e.g., Interconnect Planning Corp. v. Feil, 774 F.2d 1132, 227 U.S.P.Q. 543 (Fed. Cir. 1985). Because there is neither the suggestion nor expectation of success that can be found in the cited art, no *prima facie* case of obviousness has been established.

Because the teachings of Altman et al. would not result in the claimed invention when combined with the teachings of Zuk et al., one of skill in the art would not have an expectation of success since the invention as claimed would not be achieved in view of such teachings. Therefore, one of skill in the art would not be motivated to combine such teachings.

Applicants submit that because there is no reasonable expectation of successfully achieving the invention as claimed, there is no motivation to combine the cited references, thus, no *prima facie* case for obviousness exists. For these reasons, Applicants respectfully request that the rejection, including as it might be applied against the amended claims, be withdrawn.

Claims 25 and 26 stand rejected under 35 U.S.C. §103(a), as allegedly being unpatentable over Altman et al. in view of Zuk et al., and further in view of Schutzer et al.

Applicants traverse the rejection as it might apply to the amended claims, including claims dependent therefrom, for the reasons given below.

Applicants submit that because the cited references do not teach all the claim limitations, one of skill in the art would not be motivated to combine the reference teachings.

The Office Action alleges, in pertinent part, that Altman et al. in view of Zuk et al. is silent with respect to teaching kit instructions. The Action then provides Schutzer et al. to cure the deficiency identified in the primary references. However, Schutzer et al. does not teach that the solid surface bound monomer incorporates from solution a MHC binding peptide, an element presently recited in the claims.

Applicants submit that, in fact, the Altman et al. reference "teaches away" from the present invention. One of skill in the art would only extract from such a teaching that the MHC binding peptide is bound to the monomer when attached to the solid surface. As such, the reference does not teach the purpose of incorporation of a MHC binding peptide from solution, and thus, the purpose of Applicants' invention could not be accomplished using the teachings of the cited reference. Therefore, the reference teaches away, since the impression left to the skilled artisan is that the product would not have the property sought by Applicants. In re Caldwell, 319 F.2d 254, 256, 138 U.S.P.Q. 243, 245 (CCPA 1963).

Applicants submit, not merely as a theoretical proposition, that because the incorporation from solution is ultimately necessary *as a requisite property* of the present invention, in view of the teachings of Altman et al. becomes an impossibility.

Further, as there is no suggestion or expectation of success regarding incorporating MHC binding peptides from solution, whether Schutzer et al. teach or do not teach instruction for carrying out assays with a kit is immaterial.

It is axiomatic that one cannot simple use the Applicant's disclosure as a "blueprint" to reconstruct, by hindsight, Applicant's claim. See, e.g., Interconnect Planning Corp. v. Feil, 774 F.2d 1132, 227 U.S.P.Q. 543 (Fed. Cir. 1985). Because there is neither the suggestion nor expectation of success that can be found in the cited art, no *prima facie* case of obviousness has been established.

Because the teachings of Altman et al. would not result in the claimed invention when combined with the teachings of Zuk et al., further in view of Schutzer et al., one of skill in the art would not have an expectation of success since the invention as claimed would not be achieved in view of such teachings. Therefore, one of skill in the art would not be motivated to combine such teachings.

Applicants submit that because there is no reasonable expectation of successfully achieving the invention as claimed, there is no motivation to combine the cited references, thus, no *prima facie* case for obviousness exists. For these reasons, Applicants respectfully request that the rejection, including as it might be applied against the amended claims, be withdrawn.

Rejections Under the Judicially Created Doctrine of Obviousness-Type Double Patenting

Claims 1-19 and 23-26 stand provisionally rejected under the judicially created doctrine of obviousness double patenting allegedly over claims 1-78 of co-pending U.S. Application Ser. No. 10/782,664.

While not acquiescing to the reasoning offered in the Office Action, and to expedite prosecution toward allowance, Applicants have provided herein a Terminal Disclaimer in compliance with 37 C.F.R. §1.321(c).

For this reason, Applicants respectfully request that the rejection against claims 1-19 be withdrawn.

Claims 1-19 and 23-26 stand provisionally rejected under the judicially created doctrine of obviousness double patenting allegedly over claims 1-21 of co-pending U.S. Application Ser. No. 10/269,473.

While not acquiescing to the reasoning offered in the Office Action, and to expedite prosecution toward allowance, Applicants have provided herein a Terminal Disclaimer in compliance with 37 C.F.R. §1.321(c).

For this reason, Applicants respectfully request that the rejection against claims 1-19 and 23-26 be withdrawn.

Conclusion

Applicants submit that pending claims 1-19 and 23-26 are in condition for allowance. The Examiner is invited to contact Applicants' undersigned representative if there are any questions relating to this submission.

A check in the amount of $1150.00 is enclosed to cover a Three Month Petition for Extension of Time fee and a Terminal Disclaimer Fee. No other fees are believed due. However, the Commissioner is hereby authorized to charge any additional fees required by this submission, or make any credits or overpayments, to Deposit Account No. 07-1896 referencing the above-identified attorney docket number. A copy of the Transmittal Sheet is enclosed.

Respectfully submitted,

Date: August 8, 2007

Daryl A. Basham, J.D., Ph.D.
Registration No. 45,869
Telephone: (858) 677-1429
Facsimile: (858) 677-1465

USPTO Customer No.: 47975
Beckman Coulter, Inc.
c/o DLA PIPER US LLP
4365 Executive Drive, Suite 1100
San Diego, California 92121-2133

Purified HLA-ABC – Clone B9.12.1

PN IM0107 – 0.2 mg – Freeze-dried

For Research Use Only. Not for use in diagnostic procedures.

SPECIFICITY

HLA-A, -B, and -C are major histocompatibility complex (MHC)-class I antigens. Like other class I molecules (i.e. HLA-E, -F, -G), HLA-A, -B, and -C are hetero-dimers consisting of a 40 – 45 kDa transmembrane glycoproteic α-chain, non-covalently combined to the invariant β2-micro-globulin. All class I molecules have conserved, monomorphic domains, but are also characterized by their extensive degree of allelic polymorphism. The structure and biology of HLA molecules are reviewed in Ref. 1. MHC molecules play a central role in the immune response: They are involved in the maturation of T cell repertoire, in the activation of T lymphocytes by presentation of xenogenic peptides or in the allogenic response (1).
HLA-A, -B and -C are "classical" MHC Class I molecules and are expressed on the surface of most nucleated human cell types. The cellular distibution of Class I molecules on non-lymphoid tissues is reviewed in Ref.2.
The B9.12.1 monoclonal antibody recognizes a monomorphic epitope common to HLA-A, -B and -C molecules (3).

REAGENT

Purified HLA-ABC Monoclonal Antibody
PN IM0107 – 0.2mg – Freeze-dried

Clone	B9.12.1
Isotype	IgG2a κ mouse
Immunogen	HLA-A2 cytotoxic T-cell clone
Hybridoma	Myeloma NS1/AG.4.1 x Balb/c spleen cells
Source	Ascites fluid
Purification	Protein A affinity chromatography
Buffer	1 mg/mL bovine serum albumin in phosphate-buffered saline.

APPLICATION

Flow cytometry:
Analysis of the antigen profile of Class I HLA molecules which are expressed at the cell surface. Analysis of the tissue distribution of Class I antigens in relation to differentiation during haematopoiesis.
Not for use in the determination of HLA tissue groups.

STATEMENT OF WARNINGS

1. Specimens, samples and all material coming in contact with them should be handled as if capable of transmitting infection and disposed of with proper precautions.
2. Never pipet by mouth and avoid contact of samples with skin and mucous membranes
3. Do not use antibody beyond the expiration date on the label.
4. Do not expose reagents to strong light during storage or incubation.
5. Avoid microbial contamination of reagents or incorrect results might occur.

STORAGE CONDITIONS AND STABILITY

This freeze-dried form may be stored at 2 – 8°C until the expiration date stated on the vial label.
No preservative has been added.

REAGENT PREPARATION

Depending of usage, reconstitute with 1 mL of distilled water, with or without 0.1% sodium azide (w/v).
The reconstituted form including 0.1% sodium azide may be stored for up to one month at 2 – 8°C.
The reconstituted form without sodium azide can be stored at –20°C or less, until the expiration date stated on the vial label.
In this case, aliquotting is recommended to avoid multiple freezing / thawing cycles.

PROCEDURE

Flow Cytometry: Use 2 µg of primary antibody (10 µL of the recommended reconstituted form) per 5 x 10^5 cells in one test, or per 100 µL of whole blood.

SELECTED RESEARCH REFERENCES

1. Krensky, A.M., Clayberger, C., "Structure of HLA molecules and immunosuppressive effects of HLA derived peptides", 1996, Intern. Rev. Immunol., 13, 173-185
2. Daar, A.S., Fuggle, S.V., Fabre, J.W., Ting, A., Morris, P.J., "The detailed distribution of HLA-A, B, C antigens in normal human organs", 1984, Transplantation, 38, 287-292
3. Malissen, B., Rebau, N., Liaboeuf, A., Mawas, C., "Human-cytotoxic T cell structures associated with expression of cytolysis. I- Analysis at the clonal cell level of the cytolysis-inhibiting effect of 7 monoclonal antibodies", 1982, Eur. J. Immunol., 12, 739-747.

TRADEMARKS

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Manufactured by:
Immunotech, a Beckman Coulter Company
130, avenue de Lattre de Tassigny, B.P. 177
13276 Marseille Cedex 9, France

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